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THE CANCER CENTERS PROGRAM OF THE NATIONAL CANCER INSTITUTE

POLICIES AND GUIDELINES RELATING TO THE CANCER-CENTER SUPPORT GRANT
APRIL, 1997

INTRODUCTION

The NCI-designated cancer centers are the centerpiece of the nation's effort to reduce morbidity and mortality from cancer. They are the major source of new knowledge relating to the nature of cancer and the major source of new and more effective approaches to prevention, diagnosis, and therapy. The cancer centers are also the principal deliverers of medical advances to the patients and families needing them and the chief educators of health-care professionals and the public. An excellent cancer center is a local, regional, and national treasure, having an impact that goes well beyond its own walls into the communities it serves directly and, by the generalizable knowledge it creates, into the world at large. To defeat cancer, cancer centers must perform excellent research, turn research results into therapies or preventives, prove that these work in the clinic, educate health-care professionals about the latest advances, and reach out to underserved populations. They must do all these things together.

NCI intends its Cancer Centers Program to assist institutions in overcoming the many obstacles to cancer's conquest. The NCI has sought to enhance the potential of institutions for discovery and for the effective application of discovery to patients and people at risk for cancer. For many years the major sources of advances in cancer biology and therapy, NCI-supported centers have more recently devoted increasing resources to newly emerging areas of opportunity, such as cancer prevention. The NCI has awarded planning grants to promising institutions developing new programs, in order to promote the establishment of new centers in relatively underserved locations. Centers have developed a variety of outreach activities, so that the benefits of scientific advances can be realized broadly throughout the population. Linkages between the centers and NCI's Cancer Information Service have expedited the flow of reliable information on cancer to patients, their families, and the general population.

To strengthen the Cancer Centers Program, the Director of NCI convened an expert panel in 1996 to assess the Program and make recommendations to NCI. The report of the Cancer Centers Program Review Group (CCPRG), entitled "Renewing the Cancer Centers Program of the National Cancer Institute" (1996), contained many constructive suggestions for how NCI might better support institutions engaged in cancer research.

Among its major recommendations, the CCPRG advised the NCI:

- to foster excellence in science relating to cancer, promote multidisciplinary approaches, and facilitate the translation of new findings back and forth among laboratory, clinic, and populations;
- solutions to serve scientific activities;
- to provide increased flexibility to excellent research institutions, while demanding at the same time strict accountability through a highly competitive peer-review process;
- to provide opportunities for the creation of new centers in institutions that develop strong scientific bases.

The Report emphasized the overwhelming importance of excellence in research across a broad spectrum of scientific and medical concerns relevant to cancer. Indeed, the core of NCI's support to its cancer centers has long been for the promotion of research. To assist discovery and its translation into direct benefit to patients and the general public, the NCI has awarded cancer-center support grants (CCSG) to institutions that have a critical mass of excellent cancer-relevant scientific research. The CCSG has provided developmental and infrastructure support that, in turn, increases flexibility and responsiveness. This is particularly important now at a time of unparalleled scientific opportunity. The CCSG's focus on research has stemmed from NCI's long-held conviction that a culture of discovery, scientific excellence, and multidisciplinary emphasis generates a cascade of tangible benefits extending far beyond the gaining of new knowledge.

An NCI center's research components - the main objects of direct CCSG support - constitute a core around which is a much larger penumbra of activities - clinical care, teaching, outreach, and education. These activities extend the benefits of research directly to patients, their families, and the general public. An institution with a strong research emphasis is ideally positioned to educate professional and lay people in its own community about medical advances and to bring the fruits of discovery directly to those who need them. The promotion by cancer centers of effective outreach strategies, the fostering of cancer education, and the provision of information on cancer to professionals and the public complement the CCSG's focus on research excellence.

NCI anticipates that the greater flexibility inherent in the present CCSG guidelines will result in the funding of new centers with a greater variety of scientific agendas. It is expected, for example, that some of these centers will focus on the opportunities and needs presented by special populations. The disproportionate burden of cancer in certain minority groups is poorly understood and badly in need of attention from the research community. In order to emphasize the importance NCI attaches to outreach and education, the awarding of the "comprehensive" designation to a center is partially contingent on its willingness to enter information about its ongoing activities in these areas into a publicly available compendium of such information coordinated by NCI**.** In addition NCI is planning initiatives intended to improve strategies for outreach and education. These initiatives will be separate from the CCSG in order not to restrict them to funded cancer centers. To increase the likelihood that excellent centers will be established to serve underrepresented geographic areas or populations, additional planning-grant initiatives will assist less developed institutions in assembling a critical mass of research programs and competing for CCSG support.

This document describes the goals, policies, and procedures relating to the CCSG administered by NCI's Cancer Centers Program. NCI's current formulation of and expectations for its centers program is heavily indebted to the Report of the CCPRG. The majority of its specific recommendations have been adopted as NCI policy and incorporated into this document, often with little or no modification in language. Thus the CCPRG has had a fundamental influence on NCI's rethinking of what an NCI-sponsored cancer center should be, how it should be reviewed, and how it should relate to other centers and to the NCI. In addition to the CCPRG Report, the present statement of policies and guidelines reflects the recommendations of NCI's several advisory boards, numerous individuals within the cancer centers themselves, and NCI's leadership and staff. It is also in concordance with the expectations and intentions of the Congress as expressed during a quarter century of interest in this program.

Part I describes the general scientific, organizational, and administrative characteristics of centers that collectively determine eligibility for the CCSG. This forms the basis of the revised guidelines for submission and review of the CCSG that follow in Part II.

PART I: DESCRIPTION OF THE PROGRAM AND ITS POLICIES

1.0 History of the NCI Cancer Centers

There is a long history of national commitment to a system of integrated, multidisciplinary cancer research aimed at rapid translation of research findings into coordinated care for cancer patients. In 1960, the National Institutes of Health established the General Clinical Research Center Grants Program to provide an opportunity for universities to establish clinical research facilities. The purpose of this program was to provide a resource to enhance the quality of clinical investigation in a medical institution apart from general hospital care. A year later, in 1961, NCI announced three new grant programs that were to have a direct bearing on broadening the base of cancer research activity in the United States: the Cancer Research Facilities Grant (CRFG); Program Project Grants (PO1s) for cancer research; and Cancer Clinical Research Center Grants (PO2s or CCRCG). The intent of these funding mechanisms was to provide support for broadly based, multidisciplinary cancer research efforts.

By 1963, there was a fairly well-defined cancer centers program of approximately $6 million at 12 institutions. The activities at these centers were diverse, including research in radiation therapy, medical oncology, and surgery, as well as basic science. Little effort was made to define or organize the cancer centers, except as a category within the NCI budget, until 1968 when the National Cancer Advisory Board (NCAB) provided guidelines and the concept of the planning, or exploratory grant. Congress envisioned a regional focus for the centers program and in 1968 the House Appropriations Committee recommended that geography be considered in the establishment of new cancer centers; this has continued to be an issue of congressional interest over the years. The Cancer Centers Program of the NCI was formally conceived and established as a result of the National Cancer Act of 1971; the Act gave a broad mandate to the centers that includes research, excellence in patient care, training and education, demonstration of technologies, and cancer control. The initial model for a cancer center was drawn from several of the older, free-standing institutions: Roswell Park, Memorial Sloan-Kettering, M.D. Anderson, and Fox Chase (formerly, the Institute for Cancer Research).

In June 1973, NCI published information and guidelines for the Cancer Center Support Grant (CCSG), which had been approved in principle by the NCAB. At that time, two classes of centers were described: comprehensive and specialized. Comprehensive cancer centers were described as those conducting long-term, multidisciplinary cancer programs in biomedical research, clinical investigation, training, and demonstration, and community-oriented programs in detection, diagnosis, education, epidemiology, rehabilitation, and information exchange. Specialized cancer centers were described as those which had programs in one or more, but not

all, of the above areas in which research efforts, specialized study, or a form of patient treatment resulted in well-defined areas of emphasis. The CCSG supported a cancer research program on an "institutional" basis rather than by funding a multiplicity of individual research and project grants. This required a review of an institution's cancer research program in totality; the extent to which a center successfully integrates and promotes institutional cancer-related activities remains a principal criterion for success of an NCI-designated cancer center.

For many years up to 1996, the Cancer Centers Program classified traditional centers as either "basic," "clinical," or "comprehensive." Comprehensive cancer centers have received this special designation by NCI after competing successfully for a clinical CCSG because they meet all the criteria for comprehensiveness, which include the entire range of research functions from basic to clinical to prevention research, as well as community outreach and service activities. Clinical cancer centers conform to many but not all of the criteria for comprehensiveness and sponsor strong basic and clinical cancer research activities. Although basic cancer centers are devoted exclusively to multidisciplinary basic research activities, many are actively involved in the translation process through collaborative arrangements with other institutions, including comprehensive and clinical cancer centers and/or industry. In 1996, there were 26 comprehensive centers, 18 clinical centers, and 10 basic centers (including one cancer prevention and control center), and one consortium cancer center.

2.0 Opportunities and Challenges - 1997

Cancer centers have demonstrated that complex research strategies are feasible and that they are able to undertake novel multidisciplinary approaches to important new research opportunities. The centers are premier sites for outstanding research, as demonstrated by the large volume of investigator-initiated grants (RO1 and PO1) that NCI awards to institutions holding NCI cancer center grants. Despite this history of success, cancer centers are facing a new set of challenges, some posed by the advancement of science, some by a changing health care environment, and some by the administrative structures that govern their operation.

The NCI agrees with recent reviews by outside advisory groups that the Cancer Centers Program remains a significant component of the nation's cancer research investment and one that is worthy of continued public support. The stability and centralized support provided by the CCSG allows an institution to conduct a wide array of investigations into the etiology and treatment of cancer. In a turbulent era when clinical research must adjust to the new realities of managed care, cancer-center support is especially critical in ensuring that there is a place where cutting-edge cancer research can be conducted. And at a time when advances in science have enlarged our focus to include asymptomatic individuals for whom genetic susceptibility and early detection can play a key role in risk reduction, clinical investigations will require an even broader array of researchers and access to greater number of research participants.

3.0 Cancer Center *versus* Cancer Research Center

The great majority of NCI's direct support to cancer centers is for the furtherance of research; most of the other activities critical to a center's service mission are supported by other means, such as patient revenues, philanthropic donations, and monies from state or local governments. NCI has therefore considered whether, as recommended in the CCPRG Report, the term "cancer research center" might not be a more accurate descriptor of the activities that NCI actually reviews and funds with the CCSG. NCI's decision to retain "cancer center" as its designation[1] emphasizes the close association within NCI-funded institutions of research and other critical components, such as clinical care, education, and outreach; indeed it is this intimate association that distinguishes these centers as a group from other "cancer centers", which, whatever their credentials as dispensers of medical care, lack the strong research base that will drive progress in the years ahead. Institutions lacking their own research base can quickly follow and adopt advances developed elsewhere, but they cannot lead, as can those centers that integrate research with service.

4.0 Institutional Variety and the Cancer Center

No two cancer centers conduct research activities identically. In fact, the centers program has always exhibited impressive variety and has relied on the ability of centers to capitalize on unique research strengths. Cancer centers have developed in a number of different organizational settings. Some are independent, free-standing institutions dedicated entirely to cancer research. Others have been formed as clearly identifiable entities matrixed within academic institutions and promote interactive cancer research programs across departmental and/or university structures. Occasionally they include multiple institutions under a clear, centralized administrative and scientific leadership.

Powerful pressures generated by reforms in the health-care marketplace have recently raised organizational complexity to new levels, as many mergers and strategic alliances blur long-familiar institutional identities. In recent years NCI has favored a policy of "one cancer center per institution or per group of closely collaborating institutions." As two or more hospitals merge organizational and managerial structures across cities or counties, how to define a "single institution" is no longer so clear. The challenges in forming an NCI cancer center are very substantial, even when the center is to sit within a single institution on a geographically contiguous campus. Complexities in organization and coordination increase significantly as additional institutions are added to the center.

NCI does not wish to prejudge the kinds of administrative arrangements that will and will not succeed; indeed, it seems likely that further developments in communications technology will make

[1] The NCI designation "cancer center" in no way constrains an institution from calling itself whatever it wishes.

feasible organizational arrangements that have heretofore been difficult to coordinate. In any case, all applicants will be judged by the same scientific, organizational, and administrative criteria.

5.0 The Essential Features of an NCI Cancer Center

In face of great institutional variety the one common denominator of all successful NCI cancer centers is excellence in research. Successful cancer centers have scientifically strong research bases, organized into collaborative programs focused on cancer; from these programs new ideas are generated and multidisciplinary research is fostered. The foundation of support for the research base is investigator-initiated grants from the NIH and other funding sources that use rigorous peer review.

In addition to excellence in research, a successful center is organized and run in ways that maximize the potential of its research base and can serve to make the whole much more than the sum of its parts. There are six essential organizational and administrative characteristics:

5.1 Cancer Focus

The existence of a clearly defined scientific focus on cancer research is usually quite clear from an examination of a center's grants and contracts, by the structure and objectives of its programs, and by the nature of collaborations between fundamental researchers and others who are more directly concerned with cancer applications. NCI recognizes that many aspects of fundamental biological research are resistant to neat labels and that the cancer-relatedness of particular areas of research should be a matter of flexible interpretation.

5.2 Institutional Commitment

A strong commitment of the parent institution to the cancer center generally manifests itself in three major ways. The parent institution should recognize the cancer center as a formal organizational component and provide sufficient resources and space to insure organizational stability and fulfillment of its objectives. The organizational status of the cancer center within the institution should be comparable to that of other organizational units of similar importance within the institution. The parent institution should also provide assurance of its commitment to continuing support of the cancer center in the event of a change in directorship and have in place a well-defined plan for this eventuality.

5.3 Organizational Capabilities

The arrangements of the center for the conduct of research and the evaluation and planning of center activities should promote joint activities as well as collaborations and interactions within

and among its programmatic elements. The organizational arrangements should take maximum advantage of the parent institution's capabilities in cancer research; this is a particular challenge in a large and diverse university or when multiple institutions are included. Most successful centers have external advisory committees that provide independent input to the center director. The internal governance of a well-run cancer center generally includes processes for decision-making and priority-setting, as well as appropriate criteria and processes for determining and sustaining the membership of individual investigators in the center.

Facilities

5.4

Facilities dedicated to the center's shared resources, to the conduct of research, and to administrative activities should be appropriate and adequate to the task. All members of the cancer center need not be located physically in facilities controlled exclusively by the center, but centers are more successful in establishing a clear identity if they have a clearly identifiable physical location. Adequate administrative oversight of facilities providing shared resources is essential.

Center Director

5.5

The director should be a highly qualified scientist and administrator with the leadership experience and authority appropriate to the managing of a complex organization. The director should serve the center and its programs in this capacity on a full-time or a significant part-time basis.

Centers seem to function most effectively when the director has the following authorities: (a) Control and periodic review of appointments of individuals as members of the cancer center. The ultimate authority for determining which individuals will be productive, contributing members of the cancer center belongs to the center's director. (b) Control of faculty appointments to the cancer center and, at a minimum, joint control (for example, with a department chairman) of recruitments of individuals who are to be members of the cancer center. © Full or shared control of specific research and resource space and equipment dedicated to the cancer center; this control provides the independent flexibility to enhance and develop the research capability and resource needs of the center. (d) If the center conducts clinical research, the center director or designee must have the authority to assure adequate access to both inpatient and outpatient facilities to achieve center objectives.

Interdisciplinary Coordination and Collaboration.

5.6

There should be research activity in a variety of disciplines and a high degree of coordination, interaction and collaboration among cancer center members that enhances the productivity and quality of cancer research in the center. An actively functioning center promotes creative, innovative, high-quality, and interactive research opportunities.

6.0 Cancer Center Designations

All NCI-designated centers satisfy the six essential characteristics outlined in Section 5.0. NCI recognizes three general categories of centers:

A ***comprehensive cancer center*** has reasonable depth and breadth of research activities in each of three major areas: basic (Part I, Section 7.1), clinical (Part I, Section 7.2), and prevention, control, and population-based (Part I, Section 7.3) research AND exhibits a strong body of interactive research that bridges these scientific areas. In the area of clinical research, a comprehensive cancer center is encouraged to initiate and conduct early phase, innovative clinical trials. In order to receive recognition as an NCI-designated Comprehensive Cancer Center, the center must meet the above scientific requirements as well as provide outreach, education and information on cancer to the community it serves (See Part II, Section 6.0).

A ***clinical cancer center*** has reasonable research activities in clinical oncology, with or without research encompassing the basic and/or prevention and control and population sciences. It is possible for an institution to compete successfully for a CCSG with clinical Programs only. However, when other areas of research are present, they should be linked collaboratively to the clinical research. A clinical cancer center is also encouraged to conduct early phase, innovative clinical trials and to participate in the NCI's cooperative groups as noted above.

The unmodified term ***cancer center*** refers to a cancer center having a scientific agenda other than that of a "comprehensive" or "clinical" cancer center. Such centers may have a narrow research focus such as in basic science, population research, epidemiology, diagnosis, immunology or other areas.

All three categories of cancer centers above, whatever their designation, receive their primary research support from sources that utilize NIH peer review or equivalently rigorous procedures.

7.0 Major Research Areas of a Center

A Policy of Inclusion: The purpose of a cancer center is to take advantage of the full range of an institution's capabilities in cancer research. Institutions having significant and meritorious Programs in two or three of the areas above (basic, clinical, prevention / control / population) should, therefore, include these areas in its cancer center. It is, for example, not acceptable for an institution having both basic and clinical research activities to submit a CCSG application focusing on the basic or the clinical research area only. A major test of both institutional commitment and the quality of the center's leadership is to strengthen all major areas present within the institution.

A center's scientific activities will obviously be tailored to the needs of the particular area of science but will in all cases be characterized by excellence.

7.1 Basic Laboratory Research

There should be a reasonable breadth and depth of integrated personnel, laboratory facilities and financial support dedicated to basic research. Centers should use this base of support to promote multidisciplinary interactions between scientists engaged in basic cancer research and, where possible, to stimulate collaborations among investigators in basic and other areas. No particular organizational configuration is mandated by these guidelines. In some institutions basic research is carried out in biology groups; others incorporate basic activities within departments devoted to clinical, prevention, or population research. The organization should serve the science and be appropriate for the institution.

7.2 Clinical Research

A strong clinical research Program will derive significant research support from external sources that are peer-reviewed by the NIH standard. Clinical studies should involve relevant laboratory research whenever possible. A cancer center should be a major source of innovative clinical studies that can later be exported, for example, to NCI's cooperative groups or directly into general medical practice. In addition to fostering translation from the laboratory and conducting early proof-of-principle clinical trials, it is appropriate and desirable for cancer centers to participate in major national multicenter studies coordinated by the NCI's clinical cooperative groups. The clinical Programs of the cancer center should provide mechanisms for the transfer of technology involving the development of innovative clinical protocols, participation in the development of effective new therapies, and the timely publication of information on advances in cancer medicine. Research into the psychosocial and behavioral aspects of cancer and its treatment, as well as into aspects of disease-related quality of life, the economic assessment of interventional strategies, and the consequences of cancer survivorship are entirely appropriate areas of activity.

7.3 Prevention, Control, and Population Research

Cancer control research is the conduct of basic and applied research in the behavioral, social, and population sciences that, independently or in combination with biomedical approaches, reduces cancer risk, incidence, morbidity, and mortality (NCI Cancer Control Program Review Group, 1997). Prevention research is directed at healthy populations, including those at high risk and/or those with detectable precancerous lesions, and cancer survivors (NCI Cancer Prevention Review Group, 1997).

Cancer prevention, control, and population research includes a wide range of possible investigations on the genetic, environmental, and behavioral determinants of cancer susceptibility, risk assessment, fundamental biobehavioral mechanisms, behavioral risk factor modification, the development of improved analytic and surveillance methods, chemoprevention, diet, early detection, and survivorship. Intervention research in cancer prevention and control should be based on a foundation of strong basic, clinical, and epidemiologic research. It is in this area that centers must demonstrate their understanding of the applications of both basic laboratory and clinical research findings to populations in order to achieve the ultimate goal of a reduction in the cancer burden.

Outcomes of interest in this area of cancer research include not only preclinical (e.g. intermediate markers of carcinogenesis) and clinical (e.g. incidence of second primary cancers in survivors), but also behavioral (e.g. smoking cessation, changes in dietary behavior and screening adherence), informed decision making (e.g. genetic testing for cancer susceptibility), psychosocial (e.g quality of life), and health services outcomes (e.g. patterns of care in organized health systems and cost-effectiveness). Programs should recognize the interactions required between multiple disciplines for effective research in this area. These disciplines include but are not limited to epidemiology, medicine, genetics, health education, psychology, sociology, anthropology, economics, biostatistics, and health services research. This is the research area that allows a center to reach out to diverse communities to assure the impact of new findings; the communication and dissemination of cancer prevention and control information is both a responsibility and a subject itself for research.

It is recognized that not every cancer center will conduct research in all aspects of prevention, control and population sciences. However, most centers should be able to demonstrate grant support not only in epidemiologic, but also intervention research.

The community outreach and education networking and infrastructure of many cancer centers provides the platform from which to conduct peer-reviewed research that investigates strategies for improving outreach, education and information dissemination. It should be noted that peer reviewed, funded research grants in these areas are eligible for inclusion in the center's Programs and access to CCSG-supported shared services, like any other competitively funded research projects of the center.

7.4 Interactions Between Basic, Clinical and Prevention/Control/ Population Research

A cancer center should feature vigorous interactions across its research areas. It should facilitate the rapid transfer of promising discoveries in the laboratory to innovative applications

involving patients and/or populations, including prevention, detection, diagnosis, treatment, and survivorship. It should also facilitate the opposite movement of unique observations in patients and populations into relevant laboratory investigations. Once an opportunity is identified, a distinguishing feature of a cancer center is its ability to sustain productive cross-disciplinary interactions within the center or between elements of the center. Although the comprehensive cancer center can be expected to have a particularly rich repertoire of interactions across different areas, all cancer centers should promote collaboration among diverse elements of their membership. Productive interactions often transcend institutional boundaries and may involve outside academic or industrial organizations. Centers having only basic research components are encouraged to seek collaborations with clinical units elsewhere, with industry, or with the NCI to facilitate the translation of fundamental discoveries into tangible patient benefit.

8.0 Community Outreach, Education and Information Dissemination of Cancer Centers (Non-research Activities)

The real uniqueness of a research-oriented cancer center, particularly one with broad programs, is its dual capacity to generate new knowledge and to interact with its communities to assure that new knowledge benefits people. This interaction may occur in many ways. Centers assure that medical advances are made available to people as soon as feasible. The provision of cancer information within their communities; the establishment of formal programs for teaching, screening, therapy, or preventive interventions; the participation of center faculty in science programs for nearby school districts; the setting up of satellite clinics in underserved areas - these are a few of the ways that centers may extend their reach to patients, populations, and professionals that might otherwise not realize the benefits of scientific and medical advances. The strong interactions of NCI cancer centers with their communities provide the networking and organizational infrastructure required to conduct research aimed at improving outreach, education and information dissemination (See Section 7.3).

9.0 Research Programs

9.1 Goals.

Cancer centers exist to foster research, in part through the creation of formal **Programs**. A Program is the activities of a group of investigators who share common scientific interests and goals and participate in competitively funded research. Programs by their very nature should be highly interactive and lead to the exchange of information, experimental techniques, and ideas that enhance the individual productivity of scientists and often result in collaborations and joint publications. Ultimately the success of Programs is measured by the emergence of productive collaborations. How this is achieved will vary with the center and the needs of particular

Programs. Formal or informal planning meetings, seminars and retreats, developmental funding of selected pilot projects, new shared resources, or key recruitments may be effective ways of promoting increasing levels of interaction.

Selection of Members.
9.2

The selection of members of a center's Programs is in some ways the most critical decision made by the leadership. The functional and productive Programs that characterize successful centers are composed of individuals selected for their scientific excellence and, just as importantly, for their commitment to work together in a scientific community.

Characteristics of Programs.
9.3

Programs should be of adequate size and scientific quality, should exhibit a high degree of interaction, and should be capably led. To insure adequate size and quality, a Program must have the equivalent of at least three entire peer-reviewed and funded research projects (e.g., % $RO1_1$ + % $RO1_2$ + % $RO1_3$ = 300%) from a minimum of three separate, independent principal investigators in the proposed Program. Peer-reviewed, funded research sub-projects of larger program grants (e.g., PO1s, P50s) may be counted as separate projects.

The interactive attributes of a Program are shown most convincingly by collaborative research projects and joint publications. Colloquia, joint seminar series, and other evidence of meaningful interchange may also serve to cement interactions around related or common goals. In addition, effective leadership provides intellectual stimulation, cohesion, focus, and direction. Specific definitions of the kinds of projects that may be used to define a Program are given in Part II, Section 3.1.1.

10.0 Cancer Centers and the CCSG

Relation of CCSG to the Cancer Center as a Whole.
10.1

The many functions of a cancer center in the areas of research, patient care, education, and outreach rely on a diverse base of support including federal, state and local government, private industry and foundations, third-party payers, and private philanthropy. Within this very broad range of activities, the CCSG has a comparatively narrow focus. The CCSG is intended to provide support to the peer-reviewed research base of the cancer center within the larger institution. Although the CCSG usually accounts for a relatively small proportion of a center's operating budget, it supports an important part of the research infrastructure, stimulates innovation, and encourages interdisciplinary and collaborative research. The presence of an effective cancer center also fosters good patient care through the close association of care and research. The back-and-forth movement of research findings between basic, clinical, and

population research venues distinguishes the research-oriented cancer center from organizations dedicated only to care and service. Research in cancer centers contributes directly to the continuous advancement of services provided by the center and its close regional affiliates and offers patients options for prevention, diagnosis and treatment that may not be available elsewhere.

10.2 Sources of Flexibility in a CCSG; Rebudgeting Authority.

More specifically, the CCSG assists institutions by providing support for the research infrastructure, such as program leaders, center administration, shared resources and services, and developmental funds for new initiatives. Funds for these purposes serve to stabilize the organization and functioning of a center, provide shared resources that are not attainable through other granting mechanisms, and provide badly needed sources of flexibility that enable investigators in a cancer center to pursue new scientific opportunities as they arise.

Rebudgeting: To enhance the flexibility inherent in these grants, NCI policy permits center directors considerable authority to move funds between budget areas in response to changing needs and opportunities. The center director has the authority to increase any area up to 25% over the level approved by peer review without prior NCI approval, provided that the areas into which funds are moved were rated no less than excellent by peer review. The rebudgeting of larger amounts than this, or fund transfers into areas rated less than excellent by peer review, requires prior NCI approval[2]. All fund transfers between areas should be included in the non-competing continuation applications, along with appropriate explanation. At the time of the next competing renewal, peer reviewers will evaluate the judgment of the director in exercising this authority for rebudgeting; specifically peer review will examine those transfers between budget areas that have cumulatively resulted in significant (>10%) changes to awarded budgets (see Part II, Section 5.2.9). Competing continuation applications should therefore account for significant rebudgeting decisions, with appropriate explanations and outcome information for each.

10.3 Shared Resources and Services.

This category provides access to technologies, services, and scientific consultation that facilitate interaction and enhance scientific productivity. The establishment and support of shared services for an entire center provides a measure of stability, reliability, cost-effectiveness, and quality control that would be difficult to achieve otherwise. Center investigators with peer-

[2] Center directors are encouraged to discuss with NCI the movement of funds into areas rated less than excellent, when doing so would significantly improve the quality of an area important to the center. The need for prior NCI approval here is not meant to discourage centers from contemplating such transfers.

reviewed, funded projects are the primary beneficiaries of all shared resources and services paid for by the CCSG.

NCI's intent is that centers may propose those functions that it wishes to have funded as shared resources; the center is then responsible for defending its choices and the associated budget request before peer review. Examples of shared resources include centralized equipment; clinical data management and protocol tracking for clinical trials; research-related informatics; survey research facilities; general and specialized animal colonies; radiation facilities and services; electron microscope facilities; histology and pathology services; tissue culture; media preparation; specialized instrument shops; glassware washing; tumor procurement services; clinical pharmacology and toxicology; immunology or immunoparameters testing facilities; nucleic acid sequencing/synthesis labs; amino acid analysis; HPLC facilities; cell sorting; chemical and drug synthesis labs; radioisotope facilities; mass spectrometry labs; and research-support services such as biosafety, specialized research library services, photography and illustration, centralized word processing, and others. This is obviously not an exhaustive list and it may not even include those resources that a particular center might most keenly wish to support with CCSG funds.

10.4 Biostatistics.

This is a shared resource central to the mission of many centers, particularly those that perform clinical or population research. Its centrality to the entire enterprise implies the need for special consideration. Participation by statisticians in many collaborative activities of the cancer center is eligible for CCSG support. For example, salary support is allowable for participation in cancer-center pilot projects, for assistance to center investigators in developing research projects or analyses for publication, and for the development of methodology that is clearly and closely related to the support of specific projects within the cancer center. The CCSG is <u>not</u> intended to support independent, investigator-initiated research in statistical methodology, for which statisticians, like other scientists, should be supported by project-specific grants. Nor is it ordinarily intended to support a significant collaborative role on a funded research project of a PI, for which the statistician should ordinarily be supported by an appropriate time-and-effort allocation as a collaborator on that PI's grant. CCSG support may be particularly useful for unanticipated needs for statistical collaboration arising in the center. Peer review of a Biostatistics unit in relation to a center's activities should utilize appropriate criteria (see Part II, Section 5.2.11).

10.5 Oversight of Clinical Research: The Protocol Review and Monitoring System (PRMS).

A particularly important function for centers involved in clinical research is a mechanism for assuring adequate internal oversight of the scientific and research aspects of its clinical trials program. A cancer center should have a mechanism in place for assuring that its clinical

resources are engaged in the best way for scientific purposes. This function is complementary to that of an Institutional Review Board, which focuses on the protection of human subjects. The PRMS is not intended to duplicate or overlap the responsibilities of the IRB, nor is it intended to perform an auditing or data-monitoring function. Its focus is on scientific merit, scientific priorities and the scientific progress of the clinical protocol research of the center (Part II, Section 3.2.7.1).

Clinical trials that are part of the center and have passed traditional peer review have access to the CCSG-supported centralized resources, such as protocol and data management and biostatistics. Included are protocols supported by the various NIH mechanisms (R0ls, U0ls, U10s, P0ls, and P50s). Also included are clinical research protocols approved by the NCI's Cancer Therapy Evaluation Program or the Cancer Control Protocol Review Committee, and those funded through institutional monies and approved by the PRMS. Studies sponsored by commercial organizations (e.g., drug or device companies) are eligible to use these resources, provided that center investigators have played a major role in the conception and design of the studies and the protocol has been approved by the PRMS. The intent here is to facilitate interaction with industry for the conduct of innovative studies that result from the scientific efforts of the center. Studies originating from commercial companies with little or no conceptual or design input from center investigators are not eligible for support.

Assessing the function and effectiveness of this mechanism is an important job of peer review; specific expectations for its organization and functioning are outlined in Part II, Section 3.2.7.

11.0 Overview of the Process for Application and Review of the CCSG

Details of the application and review process are given in Part II, and only general comments are in order here. Because the essential purpose of a CCSG is to foster excellent science and productive interactions within institutions that already have substantial research bases, the application for a CCSG and the presentations during its review should be focused on demonstrating convincingly the overall excellence of the research base, the extent of the value added to the research base by CCSG support, and the strength and vigor of the leadership of the cancer center. Supporting materials should be presented in sufficient detail to convince peer review that all resource requests are justified.

Before an application is submitted, staff members of the Cancer Centers Branch may assist applicants by providing advice on a range of matters relating to the Cancer Centers Program as a whole, funding policies, and strategies for assembling a cogent and persuasive application. In

addition, all new, competing, and amended/revised applications requesting $500,000 direct costs or more must, by NIH policy, contact NCI program staff and obtain prior agreement to accept the application for review. (See Part II, Section 2.3.1)

After submission of the application, the peer-review process is overseen by a scientific review administrator (SRA), located in NCI's Division of Extramural Activities. The SRA's responsibility is to supervise the review process in a manner that ensures a technically competent and unbiased review. While the application is in review, program staff may serve as a resource to the SRA on matters relating to program policies and guidelines, in accordance with NIH policy[3].

Because the CCSG is a large grant, NIH policy stipulates that applications from institutions without a CCSG (i.e., new applications) should be preceded by NCI agreement to accept the application for consideration (Part II, Section 2.3.1). Peer review of all CCSG applications generally involves a site visit to the applicant institution, followed by consideration of the application and site-visit report by a parent committee. Following assignment of a priority score and the evaluation of the scientific requirements for comprehensiveness (Part II, Section 5.2.15) by the parent committee, action by the National Cancer Advisory Board completes the peer-review process. Final funding decisions are made by NCI's Executive Committee (EC) in accordance with its plan for the Cancer Centers Program during each fiscal year. Also, the EC will consider a center for comprehensive designation. If it has met the scientific requirements, the EC requests and reviews a summary report of the center's activities in outreach, education and information dissemination and verifies the applicant's willingness to make this information available to the community it serves and to keep information accurate and up-to-date (Part II, Section 6.0); after this review the EC makes its final decision about the awarding of the comprehensive designation to those centers.

12.0 Peer Review

The scientific merit of a center's proposal is assessed by panels of peers of the applicant. Proper review of a complex center - whether at site visits or at the deliberations of the parent committee - requires participation of excellent scientists: individuals with substantial experience, a broad perspective on cancer research, and a high degree of scientific, organizational, and administrative sophistication. Breadth is a necessary component of peer-review groups: some individuals will come from other cancer centers and will have a view from their own experience on what is required for a fully successful operation; others will participate because of their substantive scientific

[3] NIH Manual Issuance #4514 ("Role of Staff at Peer Review Advisory Committee Meetings and Exchange of Information among Review, Program, and Grant Management Staffs") describes in detail the policy that applies to all grant review at the National Institutes of Health. This document is available upon request from the Cancer Centers Branch.

expertise in particular areas of research and may come from institutions or departments having nothing to do with a cancer center. As with other investigator-initiated grant programs at the NIH, the validity of the evaluative process rests largely with the skill of peer reviewers and their willingness to spend the necessary time and energy assuring that the centers program exists for the promotion of scientific quality. Additional comments about the peer review of center grants are in Part 2, Section 5.1.

Before an application is submitted, staff members of the Cancer Centers Branch may assist applicants by providing advice on a range of matters relating to the Cancer Centers Program as a whole, funding policies, and strategies for assembling a cogent and persuasive application. In addition, all new, competing, and amended/revised applications requesting $500,000 direct costs or more must, by NIH policy, contact NCI program staff and obtain prior agreement to accept the application for review. (See Section 2.3.1).

13.0 Major Policies on Budget

13.1 Competing Continuation Applications (Type 2) - Size of Total Request.

After careful consideration, the NCI plans to continue its past policy of not imposing a rigid formula for limiting the total size of CCSG requests or awards. NCI will continue to allow centers the flexibility to develop budgets in relation to the needs of their funded research base relevant to cancer. Recent analyses show that for NCI centers the median ratio of the size of the CCSG in relation to the size of the NCI-supported research base is 0.2. While the amounts that individual institutions may be able to justify convincingly to peer review may deviate significantly from this, a ratio of 0.2 serves as a reasonable benchmark to applicants and peer reviewers on the size of total requests.

13.2 Competing Continuation Applications (Type 2) - Increases.

There are no restrictions on the allowable increase in the budget request over the last previous year. Applicants are free to request any dollar amount that they can convincingly justify to peer review. The appropriate size of a CCSG request in any competitive renewal should relate closely to the science that it is intended to support. NCI's ability to pay awarded CCSG at full recommended levels varies from year to year with the size of NCI's congressional appropriation. **Peer review** should scrutinize all budget requests carefully to assure that they are well justified. This is particularly so for applications requesting significantly more than 20% of the institution's NCI research base. As is detailed further in Part II, peer review will pay attention to <u>all</u> budgets in relation to the quality of the underlying science in the center's research base.

13.3 Competing Supplement Applications (Type 3).

Competing supplement applications are accepted by the NCI for review and consideration only under exceptional circumstances (see Part II, 2.3.3). If a supplement application is accepted by the NCI, no restrictions apply to the budget that may be requested.

13.4 First-Time Applications (Type 1).

Budget requests from a center applying for first-time funding (this includes centers that may have lost funding in the past and are reapplying without a current CCSG in place) should not exceed $850,000 (direct costs) for the first year (the budget in subsequent years will generally receive cost-of-living adjustments)[4]. Awards may be for 3-5 years, depending on what has been requested and the results of peer review. The cap on the budget request for a first-time application is largely predicated on the very limited track record of a newly applying center as an organizational entity.

14.0 Funding Policies

Peer review of new and recompeting applications over the course of a fiscal year results in a range of priority scores for approved applications. Each year NCI establishes a funding policy for the centers program that aims to separate applications deserving continued funding from those that do not. Applications with scores meriting funding are paid according to a sliding scale that rewards applicants in proportion to their priority scores. Applications judged not to merit funding will receive either no funding (new applications) or 1-2 years of phase-out funding at negotiated levels (recompeting applications). During the period of phase-out, the center will be able to revise and resubmit an amended application that addresses the concerns of peer review.

The absence of a cap to limit the size of individual awards and to control the overall budget for the centers program places a particularly heavy responsibility on the peer review process and on decision-making at NCI accompanying each year's funding plan. Peer review will play a major role in judging the merit of budget requests and in guiding the decisions of NCI about the funding of

[4] Type 1 applications from centers with a recent previous CCSG that has been phased out because of an unfundable priority score may present situations meriting special consideration. NCI will consider these cases individually as potential exceptions to the general limitation on budget requests.

individual grants. Clearly, however, other issues will factor into the ultimate decision about funding levels, such as the overall availability of funds and the need to assure entry of meritorious new centers into the program. Each year the funding plan for the cancer centers will be discussed and approved by the NCI's Executive Committee.

In years of significant budgetary constraint, funding plans will spread the impact over the entire program (non-competing as well as competing grants); this policy reduces the adverse impact on those institutions that happen to be competing during a difficult year. As funds become available in future years, restorations can be considered as appropriate.

While many institutions have had funded cancer centers for a long time, the program has exhibited a rather significant level of turnover. Sometimes a funded institution loses crucial elements of its research base or may lose one or more of the essential administrative or organizational elements. A center that has lost its CCSG may reapply and recompete successfully for CCSG funding once its deficiencies have been corrected.

15.0 The Relationship of Centers to Each Other

Cancer centers relate to each other in complex ways. They are crucial nodes in the NCI's multicenter trials programs in treatment and prevention. In the years ahead, cooperation among centers will be critical for the success of NCI initiatives in molecular and imaging diagnostics, early detection, and cancer genetics. Centers also collaborate with each other to realize common goals outside the sponsorship of NCI, as shown by the formation of voluntary consortia of centers and by joint participation in collaborative studies sponsored by private industry. On the other hand, centers also sometimes find themselves in direct competition with each other, particularly when multiple centers are located in the same geographical area.

As a support mechanism for a center's research base, the CCSG is focused on the individual cancer center. The extent to which a center's investigators use CCSG resources to enhance collaborations with scientists in other institutions will vary with time and from center to center. The NCI will not require that CCSG resources be utilized to foster specific inter-institutional activities. Nor do centers have, by virtue of a funded CCSG, implied obligations relating to joint activities with each other or with the NCI. When NCI wishes to enable investigators to take advantage of emerging opportunities that would benefit from consortial action, it will attempt to make the necessary resources available separately. Such opportunities may be in the form of administrative or competitive supplements to the CCSG if they are time-limited and within the scope of the CCSG. On the other hand, if they require substantial sums or a long timeframe to accomplish, or if they lie

outside the scope of a research-oriented infrastructure grant, independent funding vehicles will be required.

PART II: GUIDELINES FOR SUBMISSION AND REVIEW OF NEW AND COMPETING CONTINUATION APPLICATIONS FOR THE CANCER-CENTER SUPPORT GRANT

1.0 General Information

These guidelines outline the National Cancer Institute's procedures for submission, acceptance, and review of an application for a Cancer Center Support Grant (CCSG). CCSGs are provided through the P30 grant mechanism to qualified applicant institutions that wish to become NCI-designated cancer centers and have successfully met a series of competitive standards associated with scientific and organizational merit. These guidelines should be read in close conjunction with Part I of this document, which describes the philosophy, general characteristics, and major policies of the Cancer Centers Program. For more information, call or write to:

Chief, Cancer Centers Branch

Office of Deputy Director for Extramural Science

National Cancer Institute

EPN, Room 502, MSC 7383

6130 Executive Boulevard

Bethesda, Maryland 20892-7383 (for Express mail use Rockville, MD 20852)

Tel: 301/496-8531

Fax: 301/402-0181

2.0 Submission, Acceptance, and Review of Competing Applications

2.1 Eligibility

2.1.1 Research Institutions in the US

2.1.2 Not More than One CCSG Per Institution

The CCSG aims to take maximum advantage of the spectrum of resources available within a cancer-research community. Because the major purpose of a cancer center is to catalyze interactions among diverse research groups from different departments, disciplines, and orientations, different components of an institution should not submit separate CCSG applications. Applications are also accepted from closely collaborating institutions that wish

to form a center and are submitting a single application. See Part I, Section 4.0 for a discussion of some of the issues involved in consortia formation.

2.1.3 Research Base

For purposes of eligibility an applicant institution must have a **research base** of at least $3,000,000 annual direct costs of peer-reviewed, cancer-related research in the institution as a whole. If the cancer center is formed from a **consortium of institutions** (that is, if several different institutions are functioning as full participants in the center, not as affiliates), the research base of the center will be the sum of the research bases of the individual institutions making up the center. The **criterion for "cancer relatedness"** is conformity to the research project Referral Guidelines of the National Cancer Institute, which define within the NIH the areas of research appropriate for funding by the NCI. A copy of the Referral Guidelines may be obtained from the Cancer Centers Branch. For many institutions, the minimum requirement of $3M (direct) can be formed entirely from NCI peer-reviewed funded research. Funding that may and may not be applied toward the minimum is defined below. NCI staff will assist with any problems of interpretation.

For Determining Eligibility to Apply for a CCSG

2.1.3.1 The following sources of support <u>may</u> be included:

All Research Supported by the NCI. This includes all types of grants, cooperative agreements, and research contracts that support research directly and for which individuals and/or projects have been peer-reviewed. This includes the following prefixes: R01, R03, R25, R29, R35, R37, R55, P01, P50, U01, U10, K and F series awards, R18, N01, and T32.

Cancer Research Supported by Other NIH Institutes and Funding Organizations. For purposes of determining the eligibility of applicants for a CCSG, it is necessary to submit information relating to non-NCI research support <u>only</u> if the applicant's NCI support is below the minimum. Grants and research contracts from other NIH institutes, and grants from the National Science Foundation (NSF) and the American Cancer Society (ACS) can be included in the minimum if they comply with the NCI Referral Guidelines. Awards from other funding organizations that utilize a peer review and funding system equivalent to that of the NIH may also apply toward the minimum; these funding sources must be approved by the NCI or must already be on a list of approved organizations compiled by the Cancer Centers Program. Abstracts should be submitted to the Cancer Centers Program <u>only</u> for those grants and contracts which

need to be evaluated for compliance with NCI Referral Guidelines in order to meet the minimum, cancer-related, peer-reviewed research base.

2.1.3.2 The following sources of support <u>may not</u> be included:

R13 grants, awards from commercial organizations, and NCI or NIH contracts that fund primarily the production of materials and/or services in support of research.

2.2 Limitations and Dollar Caps on CCSG Applications

2.2.1 Time Limitations

CCSG awards will be for periods of up to five years. Peer reviewers may elect to recommend shorter funding periods if they believe that earlier evaluation is warranted.

2.2.2 Dollar Ceilings on New (Type 1) Applications

A new application is limited to a request for no more than $850,000 in direct costs in the first year (with cost-of-living adjustments in the non-competing years)[5]. An actual award will be based on the peer-review budget recommendation, which may be less than this maximum.

2.2.3 Dollar Ceiling (Cap) on Renewal (Type 2) and Supplemental (Type 3) Applications

There are no restrictions on the allowable increase in the budget request over the last previous year. Applicants are free to request any dollar amount that they can convincingly justify to peer review. The quality and quantity of science to be supported by the center and the projected intensity of use for shared resources should be the primary determinants of the budget request. Applicants should note below in Section 2.3.2 regarding the special circumstances for accepting and reviewing supplemental applications.

2.2.4 Page Limitations

[5] See footnote to Part I Section 13.3.

The CCSG application should be as concise as possible. Page limitations on certain individual sections of the application are detailed in Part III, which contains formatting information for the application. With these limitations, most CCSG applications will be 200-800 pages, depending on the size of the center and the breadth of research supported by the CCSG.

2.3 Submitting the Application

2.3.1 Agreement to Accept an Application

By NIH policy (NIH Guide, Vol. 25, Number 14, May 3, 1996), all unsolicited applications - new (Type 1), competing continuation (Type 2), competing supplement and amended/revised version of the preceding grant application types requesting $500,000 or more in direct costs must contact the relevant Institute and obtain agreement from Institute program staff to accept the application for review and consideration of an award. When the application is eventually submitted, it must be accompanied by a cover letter identifying the Institute staff member who agreed to accept the application. This policy requires an applicant to obtain agreement for acceptance of any such application and any subsequent amendment. In addition, if for any reason, your application is not submitted by the expected submission date, these procedures will need to be repeated for any future submission date. Because this is NIH policy, if your application does not include a cover letter that contains the required information, it will be returned to you by the Center for Scientific Review.

By NCI policy, a center applying for a CCSG must have a research base of at least $3,000,000 (annual direct costs) of peer reviewed cancer-related research (defined in Section 2.1.3). The potential applicant should contact the Chief, Cancer Centers Branch, to receive confirmation of eligibility. If the minimum research base cannot be confirmed by a simple examination of the NCI's grants database, then the applicant should provide the following additional information: (1) copies of existing documentation (e.g. award statements) of NCI-supported research projects relevant to eligibility (see section 2.1.3.1), showing the PI, grant or contract number, title, direct-cost funded level for current year and total award period; (2) copies of existing documentation of all non-NCI-supported research projects to be used to reach the $3,000,000 minimum, showing PI, funding agency, identification number of funding agency, title, direct-cost funded level for current year, and total award period. Also, copies of existing descriptions of each non-NCI-supported research projects should be provided.

The Chief, Cancer Centers Branch, will notify the potential applicant in writing that the applicant is eligible to submit a CCSG application and that NCI is willing to accept it for

review.

2.3.2 Preapplication Consultation (Optional)

At the request of a prospective applicant, NCI program staff will schedule a preapplication consultation. The consultation should be scheduled well in advance of the due date for submission and is intended to help the applicant understand the Cancer Centers Program and discuss strategies for preparing a competitive application. NCI staff will clarify the intent of the guidelines, discuss funding trends, provide generic information about CCSG applications from similar institutional settings, and describe the peer-review process. The applicant can define which issues would be most helpful to discuss and then work with NCI program staff to decide what information is most appropriate to provide. The following are examples of items that help NCI staff understand the plans of first-time applicants:

- A brief description of the background and responsibilities of the cancer center director and the key senior leaders of the center.
- A diagram showing the reporting, programmatic and advisory structure of the center and how it relates to the structure of the institution as a whole.
- A brief description of how the center expects to meet the essential organizational and administrative characteristics of an NCI-supported cancer research center.
- A brief description of the major scientific Programs and the projected leadership, participants, and criteria for selecting Program members, if these are known.
- Direct-cost budget estimates (in aggregate, not itemized) for the first year for each allowable budget category and individual shared resource.
- An addendum listing the currently active peer-reviewed research grants, cooperative agreements and contracts, grouped by the program elements that will form the entire research base of the cancer center. Typically, this listing will be longer than the research base used to meet eligibility requirements. For each project, the principal investigator, project title, direct-cost dollars for the current year, and the total project period (e.g., 05/01/96 - 04/30/01) should be listed.

2.3.3 Supplemental Applications

2.3.3.1 Competing Supplemental Applications

Competitive supplemental applications are accepted by the NCI for peer review and funding consideration only under exceptional circumstances. Because supplemental applications are particularly difficult for peer reviewers to evaluate outside the context of the overall CCSG, such applications will be accepted only when there are clear and compelling reasons for doing so. These might include, for example, a fundamental change in the parent institution of the cancer center, such as a formal merger with another health care or research institution. In all cases, the applicant must clearly establish that waiting for the next competitive renewal application cycle would have a long term affect on the success and/or progress of the cancer center. Centers wishing to submit supplemental applications should make a written request to the Cancer Centers Branch Program Director explaining the exceptional circumstances. Written approval from the Program Director to submit the supplement is required and will depend on the following: 1) the strength of the arguments presented in the request; 2) the ability of the NCI to provide peer review of the request in a timely manner; and 3) the anticipated availability of resources to pay the request should it receive a competitive score in peer review.

Supplemental applications to correct deficiencies noted previously in peer review will not be accepted.

2.3.3.2 Administrative Supplements

Depending upon the availability of funds, the NCI will consider administrative supplements to CCSGs to pursue important, short-term scientific opportunities that need immediate attention and would not be possible to initiate and sustain through the normal, competitive grant process (e.g., RO1s).

2.3.4 Evaluation of Comprehensiveness

There are no special provisions in the CCSG application format that allow an applicant to specifically apply for the comprehensive designation. If an applicant does not wish to be reviewed for comprehensive status, then he/she should so indicate in a cover letter with the CCSG application. Otherwise, the peer review of comprehensiveness will be performed by the parent review committee.

2.3.5 Key Dates in the Grant Review and Funding Process

Preapplication Consultation*	Sept/Nov	Jan/Mar	May/Jul
Application Receipt Date	Feb. 1	Jun. 1	Oct. 1
Site Visit	May/Jun	Sept/Oct	Jan/Feb
Review Committee Meeting	Jul/Aug	Nov/Dec	Mar/Apr
NCAB Meeting	Sept/Oct	Jan/Feb	May/June
Earliest Start Date	Dec. 1	Apr. 1	July 1

* Optional

If there is any difficulty in meeting receipt dates, NCI staff should be notified in advance.

2.3.6 Where to Send the Application

An original and three copies of the CCSG application should be submitted to the Center for Scientific Review (CSR), NIH, according to the instructions in the Grant Application Form-398 (5/95) kit. For a new application, this should be accompanied by a cover letter naming the NCI staff person who agreed to accept the application for consideration (Section 2.3.1).

In addition, at the same time copies are submitted to CSR, please send two complete copies under separate cover to the NCI directly; this will greatly assist NCI staff in scheduling reviews and determining whether additional information is needed for the review. The NCI address is:

Referral Officer
National Cancer Institute
Executive Plaza North, Room 636A
6130 Executive Boulevard, MSC 7405
Bethesda, Maryland 20892-7405 (for Express mail use Rockville, MD 20852)
Tel: 301/496-3428
Fax: 301/402-0275

2.3.7 Modifications After Submission

After grant submission, all correspondence should be directed to the Scientific Review Administrator. Minor, unavoidable modifications of the application can be accepted up to one month prior to the site visit without compromising the review

process. Major modifications, however, may result in deferral by the SRA to the next round of receipt and review. Additional clarifying information may be received between the site visit and the meeting of the parent committee [the NCI Initial Review Group (Subcommittee A)]. The decision on whether to accept modifications of the application or additional information or to defer the application rests with the SRA. Generally, new material should serve to clarify areas already reviewed and not represent major changes in the application as written and/or presented.

2.4 Acceptance of the Application

Upon receipt of an application, the SRA will conduct a thorough review of the submitted materials with attention to the following elements:

2.4.1 Verifying Eligibility

The first-time applicant should have already had eligibility confirmed by the Cancer Centers Branch before preparing and submitting a CCSG application. This determination is not necessary for competing renewals.

2.4.2 Conformity with Guidelines

Applications should exhibit the general organizational, administrative, and operational structure of cancer centers and request allowable and appropriate costs as outlined in these guidelines.

2.4.3 Format

Applications should be prepared in conformity with the format outlined in Part III of these guidelines to facilitate review of the submission. It is very much in the applicant's interest that review of these complex applications be as trouble-free as possible for peer reviewers.

2.4.4 Completeness of Required Information

Both Part III of the guidelines and the Standard Cancer Center Information summaries are designed to assure that an application contains all of the information necessary for an objective and thorough review. The applicant should assure that all essential information is presented completely and unambiguously, so that the quality and consistency of the review process is not compromised.

When an application reveals deficiencies in the elements 2.4.2 - 2.4.4 above, depending upon the magnitude of the problem, the SRA may exercise any of the following options: (1) request additional clarifying information or revised materials

from the applicant; (2) accept for review only those parts of the application that have been prepared in accord with the CCSG guidelines; (3) defer the application to a later review cycle; or (4) return the application to the applicant without review. In addition, peer reviewers retain the option of reducing the merit or not recommending for further consideration any element in the application that they do not feel has adequate documentation to make a full and fair judgment.

2.5 Review of the Application

Once the application is submitted, at no point in the review process should the applicant contact any member of the site-visit team, the parent review committee, or the National Cancer Advisory Board. It is a serious breach of NIH policy for the applicant to have any form of communication with reviewers between submission of the application and rendering of a funding decision.

2.5.1 Site Visit

Generally, CCSG applications are site-visited by a group of experts under the authority and responsibility of the SRA. Site visitors gather information for final evaluation by the parent committee. Typically site visits range from one to two and one half days depending upon the size and complexity of the application. Revised applications are not necessarily site visited again unless there are substantial changes in the center that require on-site information gathering.

2.5.2 Parent Committee

The National Cancer Institute Initial Review Group (Subcommittee A) (NCIIRG) is a charted review committee of the NIH. After considering the written report of the site visitors, the expressed viewpoints of NCIIRG members who participated in the site visit, and the deliberations of the full committee, the NCIIRG provides a final merit evaluation and a budget recommendation for the CCSG application in the form of a Summary Statement, which is provided to the principal investigator as soon as it is available.

2.5.3 *Ad hoc* Review

Whenever conflicts of interest can be anticipated by the SRA within the usual two-step peer review system of site visit and NCIIRG, (e.g., when applications are submitted from institutions of NCIIRG members), the SRA is obligated to conduct an *ad hoc* review. In these cases, a single-step *ad hoc* review is conducted in lieu of the usual two-step process.

2.5.4 National Cancer Advisory Board (NCAB)

The NCAB is the final step in the peer-review process. The NCAB may concur with all peer-review recommendations, ask for re-review, or make some other recommendation. NCAB approval must precede funding.

2.6 Inquiries About the Application

2.6.1 Before Completion of NCIIRG Review

After submission of the application and before completion of the site visit and the NCIIRG review, inquiries are directed to the Scientific Review Administrator, who is responsible for all aspects of the peer review process.

2.6.2 After Completion of NCIIRG Review

After the NCIIRG meeting, all inquiries should be made to the Chief of the Cancer Centers Branch (CCB) or to the program director in the CCB responsible for programmatic oversight of the application. The Grants Management Specialist is also an important source of information for all post-review fiscal matters pertaining to the grant.

3.0 Programs, Budgets, and Allowable Costs

3.1 Programs

A general description of Programs and how they are expected to function is given in Part I, Section 9.0. Peer reviewers will be asked to assess the effectiveness of a center's Programs and leaders.

3.1.1 Definition of Peer-Reviewed, Funded Research Projects for Inclusion in Programs

Peer review as employed by the NIH is the acceptable standard for inclusion of a cancer-related research project within a formal Program. Peer-reviewed, funded projects include the following:

- Awarded individual research grants, cooperative agreements and research contracts from the NCI. This includes all awards with the following prefixes: R01, R03, R18, R25, R29, R35, R37, R55, PO1 subprojects, P50 subprojects, U01, N01 research contracts and peer-reviewed, funded subcontracts of center members participating in collaborative research.
- Components of National Cooperative Groups (e.g., U10s) funded by the NCI

(consult the Cancer Centers Program staff to determine which components are equivalent to separate research projects).

- Individual research studies involving protocols approved by the NCI Cancer Therapy Evaluation Program (CTEP) and funded by NCI.
- Individual research studies involving prevention and control protocols approved by the NCI Cancer Control Protocol Review Committee and funded by NCI.
- Awarded research grants, cooperative agreements, and research contracts from other institutes of the NIH (same prefixes as above).
- Awarded research grants from the National Science Foundation.
- Awarded research support from Howard Hughes Medical Institute.
- Awarded research grants from the national office of the American Cancer Society.
- Awarded research grants from federal agencies, state and private organizations that meet the NIH standard for peer review. The updated list of eligible organizations can be obtained from the Chief, Cancer Centers Branch.

Applicants having research support from a funding agency not listed above which (s)he believes should be eligible for inclusion should consult the Cancer Centers Branch for

information on how to apply for consideration.

3.2. Allowable Budget Items

The CCSG is intended to provide reasonable costs for a great variety of activities that are clearly related to the research needs of the cancer center. The major categories of allowable costs include the following:

3.2.1 Salaries for Senior Leaders and Program Leaders

Individuals in pivotal leadership positions in the center are eligible for salary support for the time and effort they devote to its research activities. They should be in place and committed to a defined percent effort commensurate with their duties and responsibilities. The accompanying narrative describing the role and function of requested personnel should clearly justify the stated percent effort, whether or not salary is requested.

3.2.2 Salaries for Staff Investigators

Members of the center who have proven research track records and are clearly important contributors to the interactive programmatic activities of the center may receive salary from the Staff Investigator budget for their specific roles in the center. To qualify, an individual should (a) play a definable and special role in helping the center achieve its objectives that go beyond the activities implied by his/her own research support per se; (b) be a PI or co-PI on at least one peer-reviewed and funded research-project award whose review conforms to the NIH standard (see Section 3.1.1).

Peer review of the uses of Staff Investigator funds should include consideration of the special importance, as described above, of supported individuals to the center and whether the budget allocation to these individuals is commensurate with the time and effort on these activities that are not supported by other awards.

3.2.3 Planning and Evaluation

Costs of planning and evaluation might, for example, include support of a well-qualified external advisory committee; the use of *ad hoc* scientific and technical consultants when appropriate; a seminar series, when the speakers or invited participants clearly serve as consultants for the center's scientific or administrative activities, as documented by agendas and/or written evaluations; retreats designed to stimulate interdisciplinary research opportunities; and/or the conduct of regular assessments of research progress, interactions, membership participation, etc. by the senior leadership of the center. Costs for internal evaluation and priority setting processes (e.g., committees, etc.) extend only to the special roles of senior leaders and Program leaders of the center. Often the use of developmental funds (see below) is guided by the planning and evaluation activities of the center.

3.2.4 Developmental Funds

Up to 25% of a first-year CCSG budget may be devoted to this category. The developmental funds of the CCSG may be used in four ways: (a) new recruitments; (b) interim research support; (c) development of new shared resources; and (d) pilot projects. Developmental funds do not pay specifically for training (but see Sections 3.2.4.1 and 3.2.4.4). They are not intended as salary support for Program leaders (Section 3.2.1), but they may fund the salaries and research costs of individuals recruited to the center specifically for their scientific expertise.

Developmental funds may be administered flexibly by the center. In most centers the funds are held centrally, and the director is responsible for their use. Alternatively or

in addition, a director may choose to allocate part or all of this part of the budget to individual Programs for discretionary use by the Program directors in a manner consistent with the preceding paragraph.

Peer review of this part of the application will be based upon the soundness of the plan for use of the funds in each category selected and, when applicable, the demonstrated track record of the center during the previous grant period in effectively using such funds. Careful records on the deployment of developmental funds, the rationale for these expenditures, and an assessment of their consequences should be assessed by peer review at each competitive renewal. The use of developmental funds allocated to specific Programs should be judged by peer review according to the same criteria as funds administered centrally.

3.2.4.1 Newly Recruited Investigators

The purpose of this category is to promote new recruitment into independent cancer research at the institution; judicious recruitments of this kind can be expected to enhance the overall research strength of the center. Eligibility therefore includes: (1) Investigators newly recruited from outside the parent institution; in this case developmental support usually begins at the time of or very soon after arrival at the grantee institution. (2) Investigators inside the institution who, whether junior scientists or well established in other scientific areas, are entering the field of cancer research as independent investigators for the first time.

Developmental funds are not intended for support of training *per se* but may be used for recruitment packages that include any of the staff needed (e.g., technicians, graduate students, postdoctoral fellows) to initiate the research program of a new investigator. Development funds are not for the support of established cancer researchers already within the institution (for example, principal investigators on R01s or subproject leaders on P01 or P50 multicomponent grants from the NCI).

The duration of support from these funds should not exceed three years. This category should provide temporary support permitting a new cancer investigator at the institution to establish his/her scientific activities at the new center and achieve independent funding.

Competing renewal applications should include an explanation of how

developmental funds in this category were used in the previous competitive segment (previous 3 to 5 year grant period), specifying which investigators and projects were supported, the rationale for recruiting these investigators relative to the needs of the center, and to what extent these investigators were subsequently successful in attracting independent research support and/or production as evidenced by research publications.

The CCSG application should identify the kinds of individuals the center plans to recruit as part of its future plans for developing the center, but it does not need to specify particular individuals or research plans.

3.2.4.2 Interim Salary and Research Support

The intent is to permit the center director to provide partial support for up to 18 months to an investigator who has a reasonable probability of regaining independent research support in the near future. This mechanism is not intended for support of individuals who are having chronic difficulty with peer-review grant support and for whom permanent institutional funds are not available. Interim salary and support may be provided whether or not some of the salary was funded by the CCSG in the Staff Investigator category. The CCSG application should include a description of the process and the criteria used to select investigators for interim support. The use of interim salary and research support is to be reported to NCI in each non-competing continuation application. At the time of the next competing continuation, peer review will examine the uses of the interim support category and the success that individuals supported from this category have had in regaining peer-reviewed grant support.

3.2.4.3 Development of New Shared Resources

Developmental funds may be used to help develop new shared resources whenever the center recognizes the need. If funds are to help build new shared resources during the grant period, they should be included in the developmental funds budget category. If the resources are sufficiently developed to be proposed and reviewed as established resources, they should be proposed under the shared resources category.

3.2.4.4 Pilot Projects

Developmental funds may be used for pilot projects or feasibility studies preparatory to the development of an application for independent peer-reviewed support and/or to take maximum advantage of a unique research opportunity or idea. Such projects, for example, may explore a new direction for a Program, nurture an especially innovative idea, explore an unconventional hypothesis,

encourage cross-disciplinary translational research, refine a methodology, or develop new methodology. Pilot projects may be awarded to either new or **established investigators.** The support of pilot projects or feasibility studies should be of relatively short duration (e.g., 1-2 years), depending upon the nature of the research.

Many institutions have particular difficulty supporting small, hypothesis-driven early clinical trials of an exploratory nature that have no grant support of their own. See Section 3.2.8 (Protocol-Specific Research) for how the CCSG can be used to support these types of studies.

The center should have defined processes and criteria in place for awarding the use of Developmental Funds for pilot projects. The CCSG application should contain a description of the process by which the center identifies hiqh-quality proposals from investigators and the procedures and criteria by which the proposals are reviewed, funding decisions made, and projects monitored to ensure effective use of pilot-project funds. Projects should be identified with a title and awarded to an individual investigator. Renewal CCSG applications should supply information about the outcome of all projects supported by the CCSG through the pilot-project mechanism**.**

3.2.5 Center Administration

This category includes the costs necessary for central administration of resources and services required for center research activities, fiscal management of the center, and reporting activities thereof. Because administrative structures differ from center to center, the requested support should be explained and justified with some care. Requests for administrative support may include an appropriate percentage of the salary of the chief administrator, support staff for senior personnel, costs for supplies, etc. Examples of non-allowable costs include non-research educational activities, public relations, fund-raising, and grant preparation.

These costs may not duplicate services normally supported through indirect costs. For university-based centers, these costs may not replace functions and services normally provided by the institution to other comparable research units of the institution (e.g., departments). For freestanding cancer centers, the CCSG should not pay the costs of operating an institution and/or hospital or, more generally, for management of those activities and functions that are reasonably regarded as institutional responsibilities. In the event of ambiguity or disagreement about what is "reasonable," center directors should be prepared to explain to reviewers why

certain requests should not be the responsibility of the institution.

3.2.6 Shared Resources and Services

The CCSG may pay for research costs associated with centralized shared resources and services. These costs are therefore not directly identified with specific research grants; indeed, except for support of pilot projects with Developmental Funds (see Section 3.2.4.4), CCSG funds are not intended to support research activities dedicated to project-specific functions, which are paid for by research project grants. In the case of matrix centers, support for shared resources or services may be requested from the CCSG if they are not normally provided by the institution to departments or other components of the institution comparable to the cancer center.

3.2.6.1 Users of Shared Resources and Services

The primary users of shared resources and services are cancer-center investigators with peer-reviewed, funded projects; this is the standard that assures that CCSG funds are being expended to support high-quality research. However, there can also be some access by others at the discretion of the center director. This use should be justified by contributions to the overall objectives of the center in cancer research. To the extent that statements in these guidelines apply to shared resources, they only apply to the proportion of a resource or service that is paid for by the CCSG; NCI clearly recognizes that most or all of these shared resources derive a portion of their operating costs from other sources.

3.2.6.2 Operational Costs to the CCSG

There is no standard approach that applies to all shared resources and services. There are always special considerations depending upon the characteristics of the institution, the technical or non-technical nature of the resource, and the proportion of the resource paid for by sources other than the CCSG. Since the primary costs of research are supported by the peer-reviewed, funded grants and research contracts of the center, the CCSG applicant should consider the following general concerns in developing budgets for shared resources and services: (1) the need for the resource relative to the current and future peer-reviewed research activities of the center; (2) the current and projected use of the resource by multiple investigators; (3) making the resource supported by the CCSG as cost-efficient as possible; also, ascertaining that the resource is still a cost-effective center expenditure in comparison to other options (e.g., purchase orders or contracts to an outside vendor); (4) maintaining stability of the operation; (5) maintaining the quality of the service; (6) assuring accessibility of the resource or service to qualified member-investigators; (7) including the

critical consultative role performed by experts who direct selected shared resources; and (8) the proportion of the total resource operation paid for by the CCSG relative to other sources.

In general, the CCSG provides salary stability for the "fixed" costs associated with key personnel operating the resource and providing consultative services, as well as minimal supplies; "variable" costs should be supported by user fees or by other sources. The ratio of the fixed-to-variable costs will depend upon the frequency of use of the resource, as some resources will be more self-sustaining than others and will cost the CCSG less, and also upon whether the service is a support function (e.g., glass washing, media preparation), or whether it provides access to expertise and technology (e.g., DNA sequencing, transgenic mice), or to collaboration (e.g., biostatistics).

3.2.6.3 Peer Review of Shared Services

The ultimate justification for any shared resource is that it supports excellent science. Because this category contains an enormous range of resources and activities, there is no sensible way to stipulate what kinds of information should be collected and presented for peer review. Considerable latitude must be accorded applicants in making their case for support of a resource to peer review; applicants should make the

case for each shared resource in a manner that makes sense for that resource. An individual core should be evaluated in straightforward terms: (1) Does it support excellent science? (2) Does it deliver a high-quality product in a cost-efficient manner? (3) Is the budget request well supported in terms of the amount and quality of the service provided?

Recordkeeping: Appropriate records of use should be maintained for each shared resource and service. The nature of this documentation depends on the resource or service and is not specified in these guidelines. These records should be available at the time of the site visit. The Principal Investigator should provide sufficient information to peer review that reviewers can judge utilization adequately. Because reviewers' ability to judge a budget request depends on information on past and projected intensity of utilization by the scientists for whom the resource is intended, the application should provide documentation on: (1) the use of the shared resource by cancer-center investigators with peer-reviewed, funded research projects; this should include a list of each investigator using the service and estimates of usage per investigator (attribution of usage to specific grants is <u>not</u> necessary); (2) the estimated total capacity of the resource

if it were operating full-time at 100% capacity, and the total output or productivity of the shared resource over a recent 12-month period; and (3) the proportion of the total usage representing use by cancer-center investigators with peer-reviewed, funded research projects.

3.2.6.4 Public Health Service (PHS) Policy Relative to Program Income

As with all other grants issued by the PHS, if income is realized from grant-supported activities (e.g., from CCSG supported shared resources), this income must be reported in the budget/financial statements accompanying annual progress reports and on the annual financial status report. In accordance with PHS Grants Policy, the "additional cost alternative" will apply to the first $25,000 of program income. Unless approved for use otherwise, program income in excess of $25,000 will be deducted from the next year's award.

3.2.7 Protocol Review and Monitoring System (PRMS)

The purpose of the PRMS is to review the scientific merit, scientific priorities and scientific progress of the clinical protocols involving cancer patients in the cancer center facilities. The PRMS is not intended to review protocols dealing with healthy human subjects and the population sciences, e.g., genetic epidemiology studies.

3.2.7.1 Elements. The PRMS should have the following elements: (1) a qualified review and monitoring committee of sufficient size and breadth of expertise to conduct a critical, fair scientific review of institutional clinical research protocols (involving cancer patients in the cancer center facilities); (2) clear criteria for scientific review which take into account the specific rationale, study design, duplication of studies already in progress elsewhere, adequacy of biostatistical input, and feasibility for completion within a reasonable time frame; (3) clear criteria for determining whether ongoing research is making sufficient scientific progress, including adequate patient accrual rates; (4) a mechanism for overseeing the prioritization of competing protocols and thus for insuring optimal use of a center's clinical resources for scientific purposes; and (5) authority and process for initiating, monitoring and terminating all cancer clinical research protocols in the center. The PRMS is responsible for periodic review of scientific progress, i.e., the goals of the study and adequate accruals. This responsibility does not include auditing or data monitoring.

3.2.7.2 Application. The CCSG application should specify the following: (1) membership of the internal review committee; (2) internal guidelines for reviewing and monitoring research protocols; and (3) a listing of all active protocols (with accruals to date) and new protocols requesting access to CCSG shared resources.

3.2.7.3 Review. The peer reviewers of the CCSG application will review this information at the site visit and will select a representative sample of the listed protocols, specified in advance of the site visit, for detailed review.

3.2.7.4 Recommendations. The reviewers may recommend either approval, conditional approval or disapproval of the PRMS. If disapproved, institutional protocols that have not been reviewed by outside mechanisms (such as the CTEP or the DCPC Protocol Review Committees) may not have access to the CCSG-supported shared resources. In cases of conditional approval or disapproval, the peer review will articulate clearly in the Summary Statement what steps or changes are needed for full approval, along with any recommendation for options and timing of re-review by the NCIIRG.

3.2.7.5 Budget. Because of the importance of maintaining a stable, effective scientific evaluation and monitoring function for clinical protocols, the budget request to support the PRMS may include appropriate personnel, administrative support, and supplies.

3.2.8 Protocol-Specific Research

The CCSG will support up to 3 FTEs for any combination of data managers or research nurses dedicated to pilot/phase I clinical trials. The intent of these positions is to provide the cancer center with a stable core of expert staff highly qualified to take part in the conduct and completion of innovative, short-term feasibility studies originating from the center's Programs. These studies can form the basis for grant support or for phase II and III studies supported by NCI cooperative groups or industry. Oversight of this budget should be provided by the leadership of the cancer center. These positions cannot be funded until the center's PRMS (Section 3.2.7) has been approved either by peer review or by subsequent staff review after peer-review concerns are met.

3.2.8.1 Application. The application should provide specific information that demonstrates the need for these positions based on a clear track record or a convincing projected activity. The application should describe the process for the

assignment and oversight of the research nurses and data managers supported by these funds.

3.2.8.2 Review. Peer reviewers will examine the number, quality, and scientific content of pilot/phase I studies conducted and projected by the center and the adequacy of the process for prioritizing, assigning and overseeing the requested research nurses and data managers.

3.2.8.3 Relation to Industry Support. Guidance is the same as for the use of other shared resources for clinical trials (see Part I, Section 10.5).

3.2.9 Some Restrictions on Allowable Budgets

The CCSG is not intended to duplicate or replace costs normally included in the institution's indirect cost base or various services and benefits normally provided by the institution (e.g., purchasing services, personnel services, and other ancillary services) in support of other research organizations (other centers, departments, institutes, etc.). In general, CCSG funds should not be used to compensate for NIH/NCI administrative reductions of active research grants, cooperative agreements, and contracts. Signatures by the principal investigator and the business official on the face page of the CCSG application officially attest that all of the requested costs comply with these conditions. CCSG funds may not be used to pay for shortfalls in funded research projects due to overexpenditures on the funded project or NIH reductions in awards.

4.0 NIH Policies Governing Conduct of Clinical Trials

4.1 Inclusion of Women and Minorities in Clinical Trials (NIH Policy)

The provision of clear documentation about the accrual of women and minorities in clinical trials is essential. If the application is not approved in this respect, a grant award cannot be issued until a corrective plan and adequate response to the critique is submitted and approved by NCI. Under the NIH policy, clinical research is defined as "NIH-supported biomedical and behavioral research involving human subjects." The policy stipulates that: "women and members of minority groups and their subpopulations must be included in all NIH-supported biomedical and behavioral research projects involving human subjects, unless a clear and compelling justification establishes to the satisfaction of the relevant NIH institute director that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research."

When the reviewers evaluate the section of the application on the inclusion of women and minorities in clinical research, they will consider whether the accrual of women and minorities to therapeutic trials is proportionate to the general cancer patient population (nationally) and to the cancer patient population in the cancer center's primary catchment area. Reviewers will evaluate accrual to nontherapeutic trials separately using similar criteria. Although accruals to both therapeutic trials and nontherapeutic trials are important, one does not substitute for the other, and therefore the data for each type will need to be presented and assessed separately. When there is substantial under-representation, the adequacy of the institution's policies, specific activities and corrective plan that together constitute a "good faith effort" become critical in convincing peer reviewers that the institute is serious about addressing the problem and is investing the appropriate effort to correct underaccruals. In addition, if the population of the catchment area of the cancer center has limited ethnic diversity, it will be important to discuss what the institute is doing to broaden the ethnic diversity of its clinical trial accruals, since the aim of this policy is to assure that the results of clinical research are generally applicable.

For the purposes of these guidelines, the definition of racial and ethnic categories as stated in the NIH policy for inclusion of women and minorities in clinical studies will be used. The definitions are: (1) Minority Groups: American Indian/Alaska Native; Asian /Pacific Islander; Black/not of Hispanic Origin; and Hispanic. (2) Majority Groups: White/not of Hispanic origin.

4.2 Inclusion of Children in Clinical Trials (NIH Policy)

It is the policy of NIH that children (i.e., individuals under the age of 21) must be included in all human subjects research, conducted or supported by the NIH, unless there are scientific and ethical reasons not to include them. This policy applies to all initial (Type 1) applications submitted for receipt dates after October 1, 1998.

All investigators proposing research involving human subjects should read the "NIH Policy and Guidelines on the Inclusion of Children as Participants in Research Involving Human Subjects" that was published in the *NIH Guide for Grants and Contracts*, March 6, 1998, and is available at the following URL address:

http://www.nih.gov/grants/guide/notice-files/not98-024.html.

As part of the scientific and technical merit evaluation of the research plan, reviewers will be instructed to address:

--Adequacy of plans for including children as appropriate for the scientific goals of the research, or justification for exclusion.

Issues related to the implementation of this policy should be referred to the Director, OEP, OER (435-2768).

5.0 Peer Review Criteria for Competing CCSG Applications

5.1 General Guidance

Overview. The role of peer review is to assess the extent to which the center has promoted and/or is likely to promote excellence in research that may lead to a reduction in the incidence, morbidity, and mortality attributable to cancer. Successful applicants will come from institutions with strong research bases in cancer-related science. They will demonstrate to the satisfaction of peer review that their center adds tangible value to the research base already in place within the institution, and that the six essential elements of an NCI cancer center are present. Successful candidates for the *comprehensive* designation will demonstrate that scientifically excellent and well-integrated Programs are in place in each of the three major research areas and that healthy interactions between these areas are evident. Reviewers will also evaluate how well the center's leadership, organization, and processes for development and evaluation have facilitated scientific productivity, strengthened the institution's research capabilities, and enabled its investigators to take advantage of scientific opportunities over and above what would have likely taken place in the same institution without the CCSG. It is up to the center director, as principal investigator of the application, to marshall the evidence in support of the effectiveness of the center.

Reviewing Science in the CCSG. Science, not process, should be the particular focus of the review. Even when elements of organization and process are to be evaluated, such as the essential organizational elements or the ways in which flexible funds are utilized, the touchstone of success should be the scientific judgment behind or consequences of particular actions or decisions. Note that, in the context of a CCSG review, assessment of scientific quality differs importantly from the familiar peer review of individual grants. It is <u>not</u>, for example, the role of peer review to re-examine in detail individual projects that have already received fundable priority scores. Rather the scientific review of a CCSG should seek to address two major issues:

What is the overall quality of the science going on in the center and its Programs? What has been the overall quality of the contributions by the center to the advancement of cancer-related science?

What impact has the center itself had (or is it likely to have) on the quality of the science, the productivity of the scientists, and the interdisciplinary activities of the institution relating to cancer?

Thus reviewers are asked to assess the extent to which the cancer center adds value over and above what one might reasonably expect from the separately funded research efforts themselves. Have the scientific Programs been assembled and members of the center selected in a thoughtful manner that results in coherent Programs and maximizes the presence of the best cancer-related science in the parent institution as a whole? How do the different cancer-related scientific thrusts in the parent institution actually fit together in the center? From the science presented at the site visit and in the application, reviewers should assess whether the choices for center membership made by its leaders have resulted in a group of excellent scientists who are also committed to productive interactions with one another. Exactly how the applicant decides to convince the peer review process that the center is a scientific success is not stipulated by these guidelines; the responsibility for doing this lies squarely on the shoulders of the CCSG's principal investigator.

Assessing Merit in Face of Institutional Variation. The peer-review process will need to reckon scientific merit and the value-added feature of centers across a great variety of institutional settings. In any particular year small institutions compete directly with very large ones; centers organized only recently against some that have existed for decades; and institutions that have only just assembled research groups against some of the most distinguished cancer-research organizations in the world. In the presence of such diversity, NCI encourages peer review to recognize and reward scientific excellence in the variety of forms it may take. The great scope of cancer research and the non-restrictive nature of CCSG requirements should make it possible to construct scientifically excellent centers around very diverse themes. It should also be evident that scientific excellence is not synonomous with large size. Reviewers should be prepared to reward those centers that have been able to create something excellent from a science base of modest magnitude. Small institutions with limited internal resources may choose to concentrate efforts in a few specialized areas and to develop a limited number of Programs that attempt to capitalize on particular scientific strengths or the availability of special populations. Focusing in this way is to be applauded, provided, as always, that the quality of the science is excellent.

The Focus on Research. The CCSG supports directly only those functions and salaries relating to research. In each component of the application, therefore, reviewers should evaluate which functions are specifically relevant to research, as opposed to those functions which relate to institutional responsibilities of any academic organization or free-standing institution. Specifically, with respect to salaried positions for scientific leadership, reviewers should distinguish those responsibilities that pertain directly to the conduct of cancer research and are in support of the center from responsibilities that would exist within any institution regardless of the presence or absence of a cancer center.

Rewarding Risk-taking. The CCSG as a whole focuses on the peer-reviewed scientific base of a center, and many of the important parameters that define the CCSG are related to this. By definition, however, much of the building of new strength of a center comes from engaging and assisting relatively junior or inexperienced individuals. Developmental funds provide a center director with a powerful and flexible means of taking chances on people or projects for which success is not guaranteed. Many shared services can also function in this way and exert some of their most positive impact by educating investigators and enabling them to attempt things they would not otherwise have been able to do. For example, the role of a highly interactive biostatistics group in promoting the ability of investigators to formulate better clinical protocols or submit better grant proposals or better publications may have considerable impact on the quality of an institution's science. This is "value added" in the best sense.

5.2 Specific Issues for Review.

To assure stringent and fair review across the diverse range of institutions applying for CCSG support, NCI provides the following specific review criteria for reviewers to consider in evaluating the merit of the CCSG application and its key sections.

NOTE: Appropriateness of the budgetary request in relation to the research and/or services provided applies to all items below for which budget is requested.

5.2.1 Scientific Quality of Each Program [6]

(merit descriptor for each Program)

- overall scientific quality of the Program
- judicious and justifiable selection of members of the Program, based upon evidence of participation in the Program
- value added by the Program to the research efforts of its members in promoting interdisciplinary and/or translational research
- appropriateness of percent effort for Program leaders
- effectiveness of Program leaders

5.2.2 Overall Quality of the Programs

(merit descriptor)

[6]Refer to Part I, Sections 6.0 and 7.2 when evaluating the clinical research of the center.

- overall scientific quality of the Programs
- value added

5.2.3 Essential Characteristics of the Center

(merit descriptor for each)

5.2.3.1 Cancer Focus

adequacy of the cancer research focus, as judged by the content of the Programs and by the research support and publications of center members

5.2.3.2 Institutional Commitment

- the extent to which the institution has met prior commitments and provided (or plans to provide) resources to insure that the center can fulfil its objectives
- adequacy of the formal organizational status of the center and its director within the institution that insures the center's stability and fulfillment of its objectives
- the adequacy of the institution's plan to deal with a change in the directorship of the center

5.2.3.3 Organizational Capability

- effectiveness of the center's organization in taking full advantage of the institution's capabilities in cancer research and in fostering scientific interactions
- adequacy of the center's procedures for selecting new members and maintaining membership status

5.2.3.4 Facilities

- adequacy and suitability of the center's facilities in relation to its activities and objectives

5.2.3.5 Center Director

- scientific and administrative qualifications and experience of the director in relation to the center's research activities and objectives
- appropriateness of the director's time commitment to the center's research activities
- adequacy of the director's authority over and effectiveness of the director's management of center's space and research resources
- adequacy of the director's authority over and effectiveness of the director's management of appointment of new members and discontinuation of existing members
- adequacy of the director's authority over and effectiveness of the director's management of new appointments to the faculty to enhance the research objectives of the center
- in centers with clinical research activities, the adequacy of the director's authority to assure access to inpatient and outpatient facilities to achieve center's objectives

5.2.3.6 Interdisciplinary Coordination and Collaboration

- extent to which interdisciplinary activities between/among Programs have added value to scientific activities relating to cancer research in the institution
- level of translational activities within the center, including the effective movement of discoveries from the laboratory into clinical and population research activities, as well as the movement of observations in clinical and population studies back into the laboratory

5.2.4 Senior Leadership

(merit descriptor)

- qualifications and effectiveness of each senior leader in relation to his/her role in the research activities of the center
- appropriateness of the time commitment of each leader in relation to needs and objectives

5.2.5 Planning and Evaluation

(merit descriptor)

- effectiveness of external and internal advisory and evaluation activities on the development of the center's scientific activities

5.2.6 Developmental Funds

(merit descriptor)

- soundness of the plan and of the judgment exercised in use of developmental funds, taking into account all categories (Sections 3.2.4.1-3.2.4.4) for which Developmental Funds were used
- overall effectiveness of the use of developmental funds (success in gaining or regaining independent support, scientific productivity of pilot projects, etc.)

5.2.7 Protocol Review and Monitoring System

(approve, conditionally approve or disapprove)

- appropriateness of the composition of the review committee relative to its responsibilities and scientific expertise
- appropriateness of the criteria for scientific review and decision-making
- effectiveness of the committee in monitoring the conduct of clinical protocols for scientific progress, e.g., the goals of the study and adequate accruals, overseeing the prioritization of competing protocols, and closing those that are not performing adequately.

5.2.8 Protocol Specific Research

(merit descriptor)

- the appropriateness of the percent efforts requested for data managers and/or research nurses as these relate to the quality, innovation and extent of pilot/Phase I studies conducted and projected by the center.
- the adequacy of the process for setting priorities in the assignment of these research nurses and/or data managers and for overseeing the progress of the research.

5.2.9 Rebudgeting Authority of the Director

(merit descriptor)

- judgment of the director in exercising authority for significant (>10% change in any category) rebudgeting of funds from one category to another (see Part 1, Section 10.2), in response to changing needs and opportunities

5.2.10 Shared Resources and Services

(merit descriptor for each resource)

- quality of the science the resource supports
- quality of the product and cost-efficiency of the service
- justification of the budget request in terms of the amount and quality of the service provided

5.2.11 Biostatistics

(merit descriptor)

- quality of biostatistical consultation and collaboration with other center investigators, as reflected by analyses of ongoing research, collaboration in planning of research projects and preparation of publications, protocol development, participation in PRMS, and other relevant measures of participation in center activities
- appropriateness of time and effort relating to activities of the center

5.2.12 Administration

(merit descriptor)

- qualifications and effectiveness of staff in providing centralized administrative services important to the research activities of the center

5.2.13 Staff Investigators

(for each individual requested: approve, lower percent effort, disapprove)

- proven record of accomplishment
- importance to the center and contribution to its scientific activities with respect to special role in achieving center objectives beyond own research support
- extent to which the investigator's record of scientific productivity and contributions to the center justify the request for support

5.2.14 Minority and Gender

(approval, disapproval)

- appropriateness of the accrual of women and minorities to therapeutic and non-therapeutic clinical trials in proportion to the patient population nationally and within the center's cachement area
- when accrual is inadequate relative to these measures, the adequacy of the center's plan in demonstrating a good-faith effort to improve performance

5.2.15 Comprehensiveness (role of the Parent Committee)

- adequacy of the depth and breadth of basic, clinical and prevention, control and population sciences to meet reasonable scientific requirements for comprehensiveness
- evidence of strong interactive collaborations bridging these sciences

5.2.16 Overall Merit Rating of the Cancer Center

(merit descriptor)

-
- value added

5.2.17 Overall Budget Recommendation

If after evaluating all individual budget requests, reviewers believe that the total budget is excessive relative to the overall quality of the science in the center, reviewers may recommend a single cut in the overall budget without identifying specific areas for reduction.

6.0 Comprehensiveness

Although there is no separate section of the CCSG application dedicated to comprehensiveness per se, the determination of whether a cancer center will be designated as "comprehensive" by the NCI is a two-step process. The first step is a determination by peer review that the center fulfills the broad scientific and interactive requirements for comprehensiveness as described elsewhere (Part I, Section 6.0 and Part II, Section 5.2.15). Unless a center chooses not to be reviewed for comprehensiveness (see Part II, Section 2.3.4), the Parent Committee automatically will

evaluate the scientific and interactive aspects of comprehensiveness as an integral part of the overall review of the Cancer Center Support Grant. The center's overall priority score after peer review will determine whether the application will be funded, in accordance with the NCI's funding policies for the Cancer Centers Program (Part I, Section 14.0); this will trigger progression to the second level of review.

Once the NCI determines that the CCSG application will be funded, a second step involves the Executive Committee (EC) of the National Cancer Institute (NCI). Centers judged by peer review to have satisfied the scientific requirements for comprehensiveness will be asked by NCI to provide separately a brief summary that describes the institution's efforts to serve its community in each of the areas of outreach, education, and cancer information. This summary should also describe how the public can access the available information (e.g., phone, website) and contain an agreement (signed by the Center Director and appropriate institutional official) to maintain the currency and accuracy of the information. The EC will examine the summary for completeness and adequacy and make the final decision to recognize the center as comprehensive. The applicant will receive official notification in writing from the Chief of the Cancer Centers Branch as an "NCI-designated Comprehensive Cancer Center" and authorized to use the special copyrighted logo developed by the NCI that signifies this official recognition.

6.1 One-time Opportunity to Reapply for Comprehensiveness

A funded grantee that has failed to receive the comprehensive recognition from either the parent committee or the EC of the NCI will be given a one-time opportunity during the grant project period to reapply for comprehensive designation. The application would address reviewer or EC concerns and be evaluated by the Parent Committee and/or the EC for approval.